

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (previously presented) A method for treating a fluid to inactivate microorganisms which may be present therein, said fluid containing one or more components selected from the group consisting of protein, blood and blood constituents, said method comprising:
 - (a) adjusting the percentage of plasma in said fluid to a desired value;
 - (b) mixing an inactivation-effective, substantially non-toxic amount of an endogenous photosensitizer or endogenously-based derivative photosensitizer with said fluid;
 - (c) exposing said fluid to photoradiation of sufficient wavelength and energy to activate the photosensitizer, whereby said microorganisms are inactivated.
2. (previously presented) The method of claim 1, wherein said mixing step occurs after said adjusting step.
3. (previously presented) The method of claim 1, wherein said adjusting step occurs after said mixing step.
4. (previously presented) The method of claim 1, wherein said adjusting step and said mixing step occur simultaneously.
5. (original) The method of claim 1, wherein said adjusting step comprises adding a sufficient volume of a diluting solution to the fluid so that the percentage of plasma is at a desired value.
6. (original) The method of claim 5, wherein said diluting solution is saline.
7. (original) The method of claim 5, wherein said diluting solution is a buffer.

8. (original) The method of claim 5, wherein said diluting solution includes nutrients.
9. (original) The method of claim 8, wherein said diluting solution includes phosphate.
10. (original) The method of claim 5, wherein said diluting solution is a cell storage solution.
11. (original) The method of claim 5, wherein said diluting solution is an anticoagulant.
12. (original) The method of claim 5, wherein said diluting solution is a cryopreservative solution.
13. (original) The method of claim 1, wherein said adjusting step comprises washing the fluid.
14. (original) The method of claim 13 including a plurality of washing steps.
15. (original) The method of claim 1 wherein said photosensitizer is a photo-activatable compound whose photolytic products (if any) are of low or no toxicity to humans or animals.
16. (original) The method of claim 15 wherein said photosensitizer is 7,8-dimethyl-10-ribityl isoalloxazine.
17. (original) The method of claim 1 wherein said microorganisms are selected from the group consisting of bacteria, bacteriophages, and intracellular and extracellular viruses.
18. (original) The method of claim 1 wherein said microorganisms are bacteria.
19. (original) The method of claim 1 wherein said microorganisms are selected from the group consisting of HIV viruses, hepatitis viruses, sindbis virus,

cytomegalovirus, vesicular stomatitis virus, herpes simplex viruses, vaccinia virus, human T-lymphotropic retroviruses, HTLV-III, lymphadenopathy virus LAV/IDAV, parvovirus, transfusion-transmitted (TT) virus, Epstein-Barr virus, bacteriophages Φ X174, Φ 6, λ , R17, T₄, T₂, *P. aeruginosa*, *S. aureus*, *S. epidermidis*, *L. monocytogenes*, *E. coli*, *K. pneumoniae* and *S. marcescens*.

20. (original) The method of claim 1 wherein said photoradiation is light in the visible spectrum.
21. (original) The method of claim 1, wherein said photoradiation is light in the ultraviolet spectrum.
22. (original) The method of claim 1, wherein said photoradiation is light in both the visible and ultraviolet spectra.
23. (original) The method of claim 22, wherein about half the light is in the visible spectrum and about half the light is in the ultraviolet spectrum.
24. (original) The method of claim 22, wherein about one third of the light is in the visible spectrum and about two thirds of the light is in the ultraviolet spectrum.
25. (original) The method of claim 22, wherein about two thirds of the light is in the visible spectrum and about one third of the light is in the ultraviolet spectrum.
26. (original) The method of claim 1, wherein said photoradiation is of sufficient wavelength to activate 7,8-dimethyl-10-ribityl isoalloxazine in the fluid.
27. (original) The method of claim 1, wherein the percentage of plasma in said fluid is adjusted to be within about 0 to about 50 percent of the total volume of said fluid when said fluid contains platelets, red blood cells, or a combination of both.
28. (original) The method of claim 1, wherein the percentage of plasma in said fluid is adjusted to be within about 0 to about 20 percent of the total volume of said fluid when said fluid contains platelets, red blood cells, or a combination of both.

29. (original) The method of claim 1, wherein the percentage of plasma in said fluid is adjusted to be within about 0 to about 10 percent of the total volume of said fluid when said fluid contains platelets, red blood cells, or a combination of both.
30. (original) The method of claim 1, wherein the percentage of plasma in said fluid is adjusted to be within about 99 to about 80 percent of the total volume of said fluid.
31. (original) The method of claim 1 wherein said photosensitizer is added to anticoagulant and said anticoagulant is added to said fluid.
32. (original) A method of claim 1 wherein an enhancer is added to said fluid prior to exposing said fluid to photoradiation.
33. (original) A method of claim 32 wherein said enhancer is selected from the group consisting of adenine, histidine, cysteine, tyrosine, tryptophan, ascorbate, N-acetyl-L-cysteine, propyl gallate, glutathione, mercaptopropionylglycine, dithiothreitol, nicotinamide, BHT, BHA, lysine, serine, methionine, glucose, mannitol, trolox, glycerol, and mixtures thereof.
34. (original) The method of claim 1 wherein said exposing step comprises flowing the fluid containing said photosensitizer past a source of photoradiation at a rate and depth selected to ensure penetration of the photoradiation through the fluid and inactivation of the microorganisms.
35. (original) The method of claim 1 wherein said fluid and photosensitizer are contained in a container transparent to said photoradiation.
36. (original) The method of claim 35 further comprising agitating said container during said exposing step.

37. (original) The method of claim 1 wherein said adding step further comprises placing said fluid in a container transparent to said photoradiation, adding said photosensitizer to said fluid in powder form, and agitating said container.
38. (original) The method of claim 37, wherein said percentage of plasma is adjusted before placing said fluid in said container.
39. (original) The method of claim 37, wherein said percentage of plasma is adjusted after placing said fluid in said container.
40. (original) The method of claim 37, wherein said percentage of plasma is adjusted simultaneously with placing said fluid in said container.
41. (original) The method of claim 37, further comprising adding nutrients in powder form to said container.
42. (original) The method of claim 37 wherein said nutrients and photosensitizer are present in the container prior to addition of said fluid.
43. (original) The method of claim 1 wherein said fluid comprises blood constituents.
44. (original) The method of claim 1 wherein said fluid comprises whole blood.
45. (original) The method of claim 1 wherein said fluid comprises a separated blood product.
46. (original) The method of claim 1 wherein said fluid consists essentially of platelets.
47. (original) The method of claim 1 wherein said fluid consists essentially of serum.
48. (original) The method of claim 1 wherein said fluid consists essentially of plasma.

49. (original) The method of claim 1 wherein said fluid consists essentially of red blood cells.
50. (original) A method for treating a fluid containing platelets to inactivate microorganisms which may be present therein, said method comprising:
 - (a) mixing an inactivation-effective, substantially non-toxic amount of an endogenous photosensitizer with a fluid which contains platelets and a plasma content of between about 0% to about 50% of the total volume of the fluid;
 - (b) exposing said fluid to photoradiation of sufficient wavelength and energy to activate the photosensitizer, whereby said microorganisms are inactivated.
51. (previously presented) The method of claim 50, wherein said fluid contains a plasma content between about 0 to about 25% of the total volume of said fluid.
52. (original) The method of claim 50, wherein said fluid contains plasma at a volume of less than 25% of the total volume of said fluid.
53. (original) The method of claim 50, wherein said method further comprises: adding sufficient additives to the fluid so that one or more proteins present in said fluid remains biologically active after said exposing step.
54. (original) The method of claim 50, wherein said photosensitizer is 7,8-dimethyl-10-ribityl isoalloxazine.
55. (original) The method of claim 50, wherein said photosensitizer is present at a concentration of between about 1 to about 200 micromolar.
56. (original) The method of claim 50, wherein said photoradiation is between about 400 and about 500 nm.
57. (original) The method of claim 50, wherein said photoradiation is between about 100 and about 500 J/cm².

58. (original) The method of claim 50, wherein said photoradiation is between about 100 and about 200 J/cm².
59. (previously presented) A method for treating a fluid containing red blood cells to inactivate microorganisms which may be present therein, said method comprising:
 - (a) adding an inactivation-effective, substantially non-toxic amount of an endogenous photosensitizer to a fluid which contains red blood cells and a plasma content of between about 0 % to about 50% of the total volume of said fluid;
 - (b) exposing said fluid to photoradiation of sufficient wavelength and energy to activate the photosensitizer, whereby said microorganisms are inactivated.
60. (original) The method of claim 59, wherein said plasma content in said fluid is less than about 10% of the total volume of said fluid.
61. (original) The method of claim 59, wherein said plasma content is less than about 5% of the total volume of said fluid.
62. (original) The method of claim 59, wherein said photosensitizer is 7,8-dimethyl-10-ribityl isoalloxazine.
63. (original) The method of claim 59, wherein said photosensitizer is present at a concentration of between about 1 to about 200 micromolar.
64. (original) The method of claim 59, wherein said photosensitizer is present at a concentration of between about 50 to about 150 micromolar.
65. (original) The method of claim 59, wherein said photoradiation is between about 420 and about 500 nm.

66. (original) The method of claim 59, wherein said photoradiation is between about 100 and about 500 J/cm².
67. (original) The method of claim 59, wherein said photoradiation is between about 50 and about 200 J/cm².
68. (previously presented) A method for treating a fluid containing plasma to inactivate microorganisms which may be present therein, said method comprising:
 - (a) adding an inactivation-effective, substantially non-toxic amount of an endogenous photosensitizer to a fluid having a plasma content of between about 60 % to about 100% of the total volume of said fluid;
 - (b) exposing said fluid to photoradiation of sufficient wavelength and energy to activate the photosensitizer, whereby said microorganisms are inactivated.
69. (original) The method of claim 68, wherein said fluid contains about 90% or less plasma by volume.
70. (original) The method of claim 68, wherein said photosensitizer is 7,8-dimethyl-10-ribityl isoalloxazine.
71. (original) The method of claim 68, wherein said photosensitizer is present at a concentration of between about 5 to about 15 micromolar.
72. (original) The method of claim 68, wherein said photoradiation is between about 300 and about 500 nm.
73. (original) The method of claim 68, wherein said photoradiation is between about 100 and about 500 J/cm².
74. (original) The method of claim 68, wherein said photoradiation is between about 300 and about 500 J/cm².

75. (original) The method of claim 1 wherein said fluid comprises a therapeutic protein composition.
76. (original) The method of claim 1 wherein said fluid contains a biologically-active protein selected from the group consisting of: factor VIII, Von Willebrand factor, factor IX, factor X, factor XI, Hageman factor, prothrombin, anti-thrombin III, fibronectin, plasminogen, plasma protein fraction, peritoneal dialysis solutions, immune serum globulin, modified immune globulin, albumin, plasma growth hormone, somatomedin, plasminogen streptokinase complex, ceruloplasmin, transferrin, haptoglobin, antitrypsin and prekallikrein.
77. (original) The method of claim 1 wherein the activity of a biologically-active protein in said fluid is at a biologically-active level after said exposing step.
78. (original) An apparatus for inactivating microorganisms which may be present in a fluid, said fluid having a portion of the plasma removed, with an endogenous or endogenously-based derivative photosensitizer, comprising:
 - (a) a source of light that emits light of a suitable wavelength and intensity to activate the endogenous or endogenously-based derivative photosensitizer;
 - (b) means for maintaining the fluid and an effective amount of an endogenous or endogenously-based derivative photosensitizer in the light path for a sufficient time to achieve the desired level of inactivation.
79. (original) The apparatus of claim 78, wherein said means for maintaining the fluid and an effective amount of an endogenous or endogenously-based derivative photosensitizer in the light path comprises a support surface substantially parallel to said source of light.
80. (original) The apparatus of claim 78, wherein said light source comprises one or more light emitting diodes.
81. (original) The apparatus of claim 80, wherein said light emitting diodes emit light in the visible range of the spectrum.

82. (original) The apparatus of claim 78, wherein said fluid comprises blood or blood components.
83. (original) The apparatus of claim 78, wherein said photosensitizer is 7,8-dimethyl-10-ribityl isoalloxazine.
84. (original) A system for treating a fluid to inactivate microorganisms which may be present therein with an endogenous or endogenously based photosensitizer comprising:
- (a) a container comprising said fluid having a reduced level of plasma, at least an effective amount of an endogenous photosensitizer or endogenously-based derivative photosensitizer, and optionally one or more additives, said container having a surface sufficiently photopermeable to allow exposure of the fluid therein to an amount of photoradiation sufficient to activate the photosensitizer;
 - (b) at least one photoradiation source in light communication with said container, said source capable of generating a suitable wavelength and intensity to activate the endogenous photosensitizer or endogenously-based derivative photosensitizer whereby microorganisms present are inactivated.
85. (original) The system of claim 84, wherein said photosensitizer is 7,8-dimethyl-10-ribityl isoalloxazine.
86. (original) The system of claim 84 wherein said photoradiation source provides light in the visible spectrum.
87. (original) The system of claim 84, wherein said photoradiation source provides light in the ultraviolet spectrum.
88. (original) The system of claim 84, wherein said photoradiation source provides light in both the visible and ultraviolet spectrum.

89. (original) The system of claim 84 also comprising a photoradiation enhancer.
90. (original) The system of claim 89 wherein said photoradiation enhancer comprises a reflective surface.
91. (original) The system of claim 84 comprising a light guide for conducting photoradiation from said photoradiation source to said photopermeable container.
92. (original) The system of claim 84 also comprising a temperature monitor.
93. (original) The system of claim 84 also comprising one or more temperature controllers.
94. (original) The system of claim 93 wherein said temperature controller is a fan directed so as to cool the light source and/or the fluid.
95. (original) The system of claim 84 also comprising means for flowing said fluid into and out of said container.
96. (original) The system of claim 84 also comprising means for agitating said fluid.
97. (original) A system for inactivation of microorganisms in a fluid containing such microorganisms comprising:
 - (a) means for adjusting the plasma content of said fluid;
 - (b) means for mixing an effective amount of an endogenous photosensitizer or endogenously-based derivative photosensitizer with said fluid in fluid communication with said means for adjusting the plasma content of said fluid;
 - (c) a photopermeable container for said fluid in fluid communication with said means for adding photosensitizer and said means for adjusting the plasma content having a depth and length selected to allow exposure of the fluid of step (b) therein to an amount of photoradiation sufficient to activate the photosensitizer at a selected flow rate;

- (d) means for producing said selected flow rate of said fluid through said container; and
 - (e) at least one photoradiation source in light communication with said container, said source capable of providing sufficient photoradiation to the fluid in said container of a type and amount selected to activate the photosensitizer.
98. (original) A system for treating a fluid to inactivate microorganisms which may be present therein comprising:
- (a) means for adjusting the percentage of plasma in said fluid;
 - (b) means for adding an effective amount of endogenous or endogenously-based photosensitizer to said fluid;
 - (c) a photopermeable container for said fluid of depth which allows exposure of the fluid to an amount of photoradiation sufficient to activate the photosensitizer;
 - (d) means for agitating said container;
 - (e) at least one photoradiation source for providing sufficient photoradiation to the fluid in said container of a type and amount selected to activate the photosensitizer.
99. (original) The system of claim 98 wherein said photopermeable container is a transparent plastic bag.
100. (original) The system of claim 99 wherein said photopermeable container is a transparent rigid plastic container.
101. (original) The system of claim 98 wherein said means for agitating said container comprises a shaker table.
102. (original) The system of claim 98 wherein said photopermeable container contains said photosensitizer prior to addition of said fluid.

103. (original) The system of claim 98 wherein said means for adjusting the level of plasma in said fluid comprises a suitable amount of a solution contained in said container.
104. (original) A method for collecting a fluid with reduced levels of microorganisms that may be present therein, said fluid containing one or more members of the group consisting of: blood and blood components, comprising:
- (a) placing said fluid in a photopermeable container;
 - (b) adding an endogenous or endogenously-based derivative photoactive material to said container;
 - (c) adjusting the level of plasma in said fluid to a desired level;
 - (d) exposing said fluid to radiation of a sufficient wavelength and intensity to activate said photoactive material, whereby microorganisms are inactivated.
105. (original) The method of claim 104 wherein said photoactive material is present in said container prior to placing said fluid therein.
106. (original) An apparatus for collecting a fluid with reduced levels of microorganisms that may be present therein, said fluid containing one or more members of the group consisting of: blood and blood components, comprising:
- (a) a photopermeable container containing an endogenous or endogenously-based derivative photoactive material and a suitable volume of a solution for adjusting the level of plasma in the fluid to a desired level;
 - (b) a light source in light communication with said container that emits light of a suitable wavelength and intensity to inactivate microorganisms which may be present in said fluid.
107. (original) A method for treating a fluid to inactivate microorganisms which may be present therein, said fluid containing one or more components selected from the group consisting of protein, blood and blood constituents, said method comprising:
- (a) removing a desired amount of the bilirubin present in the fluid;

- (b) adding an inactivation-effective, substantially non-toxic amount of an endogenous photosensitizer or endogenously-based derivative photosensitizer to said fluid;
 - (c) exposing said fluid to photoradiation of sufficient wavelength and energy to activate the photosensitizer, whereby said microorganisms are inactivated.
108. (original) A blood product comprising inactivated microorganisms and endogenous photosensitizer or endogenously-based derivative photosensitizer and a lowered plasma content than occurs naturally, made by the method of claim 1.